

We claim:

1. A method for extended and controlled delivery of parathyroid hormone to a patient in need thereof comprising:
implanting a medical device into the patient, the medical device comprising a substrate, a plurality of reservoirs in the substrate, a release system contained in each of the reservoirs, wherein the release system comprises parathyroid hormone; and
controllably releasing a pharmaceutically effective amount of the parathyroid hormone from the reservoirs.
2. The method of claim 1, wherein the step of controllably releasing provides intermittent release of the parathyroid hormone.
3. The method of claim 1, wherein the parathyroid hormone is released daily in intermittent doses of between about 10 and 300 µg.
4. The method of claim 3, wherein the daily intermittent doses are released over a period of ten months or more.
5. The method of claim 1, wherein the parathyroid hormone is released in a pulsatile manner, each pulse having a duration of less than four hours.
6. The method of claim 1, wherein the pharmaceutically effective amount of the parathyroid hormone, released over a first period of time, is effective to form bone tissue.
7. The method of claim 6, further administering a pharmaceutically effective amount of a bone resorption inhibitor, released over a second period of time, to maintain bone tissue at a level present after the first period of time.
8. The method of claim 7, wherein the bone resorption inhibitor is selected from the group consisting of bisphosphonates, selective estrogen receptor modulators, calcitonins, vitamin D analogs, and calcium salts.

9. The method of claim 6, wherein the bone resorption inhibitor is administered orally.
10. The method of claim 6, wherein the bone resorption inhibitor is released from reservoirs of the medical device.
11. The method of claim 1, wherein the patient is a female and the step of implantation of the medical device comprises inserting the medical device into the vagina of the patient.
12. A implantable device for the extended, controlled delivery of parathyroid hormone to a patient in need thereof comprising:
a substrate;
a plurality of reservoirs in the substrate;
a release system contained in each of the reservoirs, wherein the release system comprises parathyroid hormone; and
a control means for selectively releasing a pharmaceutically effective amount of the parathyroid hormone from each of the reservoirs.
13. The device of claim 12, which is able to release a pharmaceutically effective amount of parathyroid hormone once daily over a period of at least six months.
14. The device of claim 12, further comprising at least one reservoir which contains a second release system comprising a drug other than parathyroid hormone.
15. The device of claim 14, wherein the drug is an anti-resorptive agent.
16. The device of claim 12, wherein each of the reservoirs contains between about 10 and 300 µg of parathyroid hormone for release.

17. The device of claim 12, wherein the plurality of reservoirs comprises 300 or more reservoirs, each containing a release system comprising parathyroid hormone.
18. The device of claim 12, wherein the release system comprises parathyroid hormone in combination with a pharmaceutically acceptable excipient.
19. The device of claim 12, wherein the release system comprises parathyroid hormone suspended in a non-aqueous vehicle.
20. The device of claim 18, wherein the parathyroid hormone is dried or lyophilized with an excipient that promotes re-dissolution upon release.
21. The device of claim 18, wherein the excipient comprises polyethylene glycol having a molecular weight between about 100 and 10,000 Daltons.
22. The device of claim 12, wherein the control means comprises reservoir caps covering the release system of the reservoirs.
23. The device of claim 22, wherein the control means further comprises means for actively disintegrating or permeabilizing the reservoir caps.
24. The device of claim 23, wherein means for actively disintegrating comprises a power source for passing an electric current or potential through the reservoir caps.
25. The device of claim 24, wherein the reservoir caps comprise an electrically conductive material and are electrically connected to an electrical input lead and to an electrical output lead, and the means for actively disintegrating the reservoir cap comprises means for selectively applying an electrical current through the reservoir cap, via the input lead and output lead, in an amount effective to heat the reservoir cap to cause the reservoir cap to disintegrate to permit release of the parathyroid hormone.

26. The device of claim 24, wherein the means for actively disintegrating the reservoir cap comprises a cathode, a microprocessor, a timer, and a demultiplexer, and wherein the reservoir caps each comprise an anode and upon application of an electric potential between the cathode and anode the reservoir cap disintegrates to permit release of the parathyroid hormone.

27. The device of claim 12, further comprising a sensor.

28. The device of claim 27, wherein the sensor measures plasma calcium.

29. The device of claim 12, wherein the control means comprises multiple layers of release system having different compositions.

30. The device of claim 29, wherein a first two or more of the multiple layers comprise the parathyroid hormone dispersed throughout a solid matrix material comprising a water soluble polymer, and a second two or more of the multiple layers comprise the solid matrix material without parathyroid hormone, each of said first two or more layers being stacked alternately with said second two or more layers.

31. The device of claim 29, wherein said multiple layers comprises a first layer having a first concentration of parathyroid hormone therein, and a second layer having a second concentration of parathyroid hormone therein which is greater or less than the concentration in said first layer.

32. The device of claim 12, capable of vaginal administration of the parathyroid hormone.

33. The device of claim 32, wherein the substrate comprises a ring-shaped or rod-shaped body.

34. A implantable device for the extended, controlled delivery of parathyroid hormone to a patient in need thereof comprising:

- a body;
- a plurality of reservoirs in the body;
- a release system contained in each of the reservoirs, wherein the release system comprises parathyroid hormone;
- a electrically conductive reservoir cap covering each reservoir;
- conducting leads to and from each reservoir; and
- a power source and a controller for selectively delivering an electric current through the reservoir cap effective to rupture the reservoir cap and release a pharmaceutically effective amount of the parathyroid hormone from the reservoir.

35. The device of claim 34, wherein the release system comprises multiple layers of release system having different compositions.